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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/678,650	10/06/2003	Regine Hakenbeck	012627-037	7623

21839 7590 03/20/2007

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POST OFFICE BOX 1404
ALEXANDRIA, VA 22313-1404

EXAMINER	
WILDER, CYNTHIA B	
ART UNIT	PAPER NUMBER
1637	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/678,650	HAKENBECK, REGINE	
	Examiner	Art Unit	
	Cynthia B. Wilder, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *15-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/403,609.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/6/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I; claims 1-14 and SEQ ID NOS: 7-13 and 18-19 in the reply filed on 10/3/2006 is acknowledged. The traversal is on the ground(s) that examining the sequences of SEQ ID NOS 7-13 and 18-19 together would not impose a serious burden to the examiner because these sequences corresponds to probes that bind a limited number of related genes that control resistance and sensitivity. Applicant asserts that the sequences of SEQ ID NOS: 7-8 are sensitivity-specific probes for PBP2x. Applicant notes to the Examiner that SEQ ID NOS: 1-6 and 14-17 were examined together in a previously related application. Like, SEQ ID NOS: 7-8, previously examined SEQ ID NOS: 1-6 are specific for PBP2x. Applicant states that SEQ ID NO: 13 is sensitivity specific probe for PBP2b. Applicant states that many issues that might arise in the present application have been well developed during examination of the parent application, which will further reduce the burden upon the Examiner in considering SEQ ID NOS: 7-13 and 18-19. All of the arguments have been thoroughly reviewed and considered. The examiner maintains that the sequences are structurally and functionally distinct one from the other. However, upon further review, the examiner will search the sequences of SEQ ID NOS: 7-13 and 18-19 with the claims 1-14 of Group I. The claims 15-17 are withdrawn from consideration as being drawn to a non-elected invention. The requirement is still deemed proper and is therefore made FINAL.

Specification

2. The specification is objected to because not all of the sequences listed at the top of page 3 are represented by a sequence identifier (SEQ ID NO:). It appears that the sequences are to be listed at SEQ ID NO: 14-17. However, there are 8 sequences recited.

Claim Rejections - 35 USC § 112: Enablement

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1, 2, 4, 6-10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are drawn to a method for identifying antibiotic resistance in bacteria comprising the step of hybridizing with at least one sensitivity-specific DNA probe and at least one resistance-specific DNA probe wherein the sensitivity-specific probes are selected from SEQ ID NO: 7-13 and differ therefrom by one to four nucleotides (Claim 2) and wherein the resistance-specific probes are selected from SEQ ID NO: 18-19 and differ therefrom by one to four nucleotides (Claim 4).

While the specification is enabling for the method of identifying penicillin resistance in *Streptococcus pneumoniae* using probes selected from SEQ ID NO: 7-13 and SEQ ID NO:18-19, the specification does not enable one skilled in the art to which it

pertains or with which it is most nearly connected to make or use the invention commensurate in scope with the claims. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirements and whether undue experimentation would be required to make and use the claimed invention (see *In re Wands*, 858 F. 2d 731, 737, 8 USPQ 2d 1400, 1404, 1988). These factors include but are not limited to:

Breadth of the Claims

The claims are written so broadly so as to encompass all antibiotics, a very large genus of bacteria and an enormous genus of oligonucleotide sequences i.e. SEQ ID NO: 7-13 and SEQ ID NO: 18-19 and oligonucleotides which differ therefrom by one or several nucleotides. The specification teaches a method for identifying penicillin resistance in *Streptococcus pneumoniae* comprising the step of hybridizing with penicillin resistance-specific DNA probes i.e. SEQ ID NO: 18-19, and penicillin sensitivity-specific probes i.e. SEQ ID NO: 7-13 and the specification teaches SEQ ID NO: 7-13 and SEQ ID NO: 18-19 (see pages 3 and 4) but the specification does not teach the method for identifying resistance to all antibiotics in any bacterium using the enormous species of claimed DNA probes. While the specification is enabling for the method for identifying resistance to one antibiotic, i.e. penicillin, in one bacterium i.e., *Streptococcus pneumoniae*, by hybridization with SEQ ID NO: 7-13 and SEQ ID NO:18-19, the specification is not enabling identifying resistance to all antibiotics in the large

genus of bacteria using the enormous species of claimed DNA probes. Therefore, the specification is not enabling for the broadly claimed invention.

Nature of the Invention

The nature of the invention is such that identifying antibiotic resistance by hybridization with DNA probes would require a teaching of a relationship between the antibiotic resistance and the claimed DNA probes wherein the teaching would minimally include an illustration or examples of the relationship between resistance to antibiotics in a variety of bacterial species and the DNA to which the claimed DNA probes hybridize. The specification does not teach a relationship between resistance to antibiotics in bacteria and the *enormous* genus of claimed DNA probes. The specification teaches a method for identifying penicillin resistance in *Streptococcus pneumoniae* comprising the step of hybridizing with SEQ ID NO: 7-13 and SEQ ID NO: 18-19 (page 3 and 4). However, the specification does not teach the enormous genus of claimed probes i.e., any probe that may be sensitivity-specific or resistance-specific or any oligonucleotides which differ from SEQ ID NO: 7-13 and SEQ ID NO: 18-19 by one or several nucleotides; the specification does not teach identifying penicillin resistance using the enormous genus of claimed probes other than SEQ ID NO: 7-13 and 18-19; and the specification does not even suggest which, if any of the claimed DNA probes would identify resistance to antibiotics. While the specification teaches a relationship between penicillin resistance in *Streptococcus pneumoniae* and SEQ ID NO: 7-13 and SEQ ID NO: 18-19, the specification does not teach a relationship

between antibiotic resistance in bacteria and the enormous genus of claimed DNA probes which would enable one of skill in the art to make and use the invention as claimed.

State of the Art

The state of the art is such that identifying antibiotic resistance in bacteria is antibiotic-specific, bacteria-specific, and gene sequence-specific as taught by Dubuc et al. (WO96/08582. 21 March 1996, page 38, Table 8). The specification teaches a method for identifying resistance to one antibiotic i.e. penicillin, in one strain of bacteria i.e. *Streptococcus pneumoniae*, using sequence-specific probes from one gene i.e. PBP comprising resistance-specific DNA probes SEQ ID NO: 18-19 and sensitivity-specific DNA probes SEQ ID NO: 7-13. Therefore, in view of the state of the prior art wherein identifying antibiotic resistance is antibiotic-specific, bacteria-specific, and gene sequence-specific, the specification does not enable one of ordinary skill in the art to make and use the invention as claimed.

Level of Predictability in the Art

The level of predictability in the art with regard to oligonucleotide hybridization using probes, which differ by one or several nucleotides, is very low. It was well know in the art at the time the claimed invention was made and the specification teaches that oligonucleotide hybridization is dependent upon complementation between the target and the probe, AT/CG content and hybridization conditions (page 6). Therefore, identification of antibiotic resistance using hybridization is dependent upon

complementation between the target and the probe, AT/CG content and hybridization conditions. Because oligonucleotide probes which differ by one or several nucleotides would differ in complementation to the target and differ in AT content, hybridization using the enormous genus of claimed DNA probes may or may not identify antibiotic-specific targets and therefore may or may not identify antibiotic resistance. Therefore, because the level of predictability in the art is very low with regard to hybridization using the enormous species of claimed DNA probes, the level of predictability in the art is very low with regard to identifying antibiotic resistance in bacteria using the claimed probes

Existence of Working Examples

The specification teaches a method for identifying penicillin resistance in *Streptococcus pneumoniae* comprising the step of hybridizing with penicillin resistance-specific DNA probes and penicillin sensitivity-specific probes and the specification teaches SEQ ID NO: 7-13 and SEQ ID NO: 18-19 and the specification teaches identification of penicillin resistance using PCR amplification. However, the specification does not teach working examples of the broadly claimed invention i.e. identifying resistance to all antibiotics in any bacterium using an enormous genus of DNA probes. Therefore, the specification does not provide working examples of the claimed invention which would enable one of ordinary skill in the art to make and use the invention as claimed.

Quantity of Experimentation Required

In view of the breadth of the claims being drawn to identifying resistance to a large genus of antibiotics in a very large genus of bacteria using an enormous genus of DNA probes; in view of the nature of the invention in which identifying antibiotic resistance in bacteria would require a teaching of a relationship between resistance to antibiotics in the large genus of bacteria and the enormous genus of claimed DNA probes and the lack of such a teaching in the specification of the relationship; in view of the state of the art in which identification of resistance to antibiotics is antibiotic-specific, bacteria-specific, and gene sequence-specific; and in view of the lack of working examples of the broadly claimed invention, it would require undue experimentation for one skilled in the art to make and use the invention as claimed.

Claim Rejections - 35 USC § 112: Written description

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2 and 4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are broadly drawn to a method for testing Streptococcus pneumonia for resistance to penicillin, the method comprising hybridization procedures using at least one sensitivity specific probe selected from SEQ

ID NOS: 7-13 and at least one resistance specific probe selected from SEQ ID NO: 18 and 19 and sequences which differ from said sequences by one to four nucleotides. The recitation of "sequences which differ from said sequences by one to four nucleotides" encompasses a large genus of nucleic acid sequences that have not been described or disclosed anywhere in the instant specification. Not only are the plethora of oligonucleotide sequences encompassed by the claimed invention as recited in the claims 2 and 4 not described, but the specification also does not provide any disclosure which supports the use of any oligonucleotide sequences comprising any modifications be applicable in the method of testing for *Streptococcus Pneumoniae* resistance. The specification supports the use of the probe sequences as described in SEQ ID NOS: 7-13 and 18-19. Based on the lack of support for the claimed invention, the specification would not have suggested to the skilled artisan that the applicant was in possession of the claimed invention as of the filing date of the application.

Second paragraph of 35 U.S.C. 112: Indefinite

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claims 1-14 are indefinite in Claim 1 for the recitations "sensitivity-specific DNA probes" and "resistance-specific DNA probes" because it is unclear how the "sensitivity"

and "resistance" relate to the "probes". It is suggested that Claim 1 be amended to clarify e.g. replace "sensitivity-specific DNA probes" with "DNA probes which hybridize to penicillin sensitive strains" and replace "resistant-specific DNA probes" with "DNA probes which hybridize to penicillin resistant strains".

(b) Claims 2 and 4 are indefinite in the recitation "probes are selected form the following oligonucleotides...." Because it is unclear whether the claims are limited to probes consisting of SEQ ID NO: 7-13 (clm 2) and/or probes consisting of SEQ ID NO: 18-19 (clm 4) or probes comprising SEQ ID NO: 7-13 or SEQ ID NO: 18-19 and sequences which differ from said sequences by one to four nucleotides. Clarification is required.

(c) Claim 7 is indefinite at the recitation of "stringent conditions" because the definition at page 5 is ambiguous and it cannot be determined what hybridization conditions is required for the instant invention. It is suggested inserting the hybridization condition into the claims.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claim 1 and 6 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Springer et al. (U.S. Patent No. 6,015,666, filed 7 June 1995).

Regarding Claim 1, Springer et al. disclose a method for identifying antibiotic resistance in bacteria comprising: isolating bacterial DNA and hybridizing the DNA with at least one sensitivity-specific DNA probe (Primer 4) and at least one resistance-specific DNA probe (Primers 1-3)(Column 5, lines 42-65).

Regarding Claim 6, Springer et al. disclose the probes are labeled radioactively (Column 6, lines 49-56).

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1 and 6 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Dowson et al. (Proc. Natl. Acad. Sci. USA, 1990, 87: 5858-5862).

Regarding Claim 1, Dowson et al. disclose a method for identifying antibiotic resistance in bacteria comprising: isolating bacterial DNA and hybridizing the DNA with at least one sensitivity-specific DNA probe (Pn12) and at least one resistance-specific DNA probe (Pn11 and Pn13) (page 5859, right column second full paragraph), wherein the bacteria is Streptococcus pneumoniae (page 5859, right column second full

paragraph) and wherein the antibiotic resistance is a penicillin resistance (Abstract and page 5859, right column second full paragraph).

Regarding Claim 6, Dowson et al. disclose the method wherein the probes are labeled radioactively (page 5859, right column, lines 4-6). Therefore, Dawson meets the limitations of the claims recited above.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 2-3, 11, 12 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dowson et al. (Proc. Natl. Acad. Sci. USA, Aug. 1990, 87: 5858-5862) as applied to Claim 1 above and further in view of Kell et al (Infection and Immunity, vol. 61, No. 10, pages 4382-4391, 1993).

Regarding Claims 4, 5, 10 and 11, Dowson et al. teach a method for identifying penicillin resistance in bacteria comprising: isolating bacterial DNA and hybridizing the DNA with at least one sensitivity-specific and at least one resistance-specific probe (page 5859, right column, second full paragraph). Additionally, they teach that the PBP genes in penicillin sensitive and resistant strains of *S. pneumoniae* comprise highly conserved regions alternating with highly divergent regions (Abstract). Dowson et al. do not teach the sensitivity-specific probes are selected from SEQ ID NO: 7-13 and the

resistance-specific probes are selected from SEQ ID NO: 18-19 or sequences that differ from said sequences by one to four nucleotides.

Kell et al. teach the PBP2x gene sequence of penicillin-resistant pneumococci and sequences which confer antibiotic resistance to pneumococci in patients wherein said sequence comprises the sequence of SEQ ID NO: 8 (see accession number z21803 and Figure 4). Kell et al distinguishes between sequences of pneumococci that resistant and susceptible to penicillin (see page 4388). Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the PBP2x gene sequence differences between antibiotic sensitive and antibiotic resistant strains and to use probes which hybridize to those sequences in the method of Dowson et al. for identifying antibiotic resistant bacteria for the obvious benefit of identifying clinically important antibiotic-resistant bacteria efficiently and economically using DNA hybridization and antibiotic response-specific probes.

Conclusion

14. No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Patent Examiner
Art Unit 1637

3/15/2007